UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/880,609	06/12/2001	Shuyuan Zhang	INRP:081USD1	7626

7590 10/03/2003

Steven L. Highlander
FULBRIGHT & JAWORSKI L.L.P.
Suite 2400
600 Congress Avenue
Austin, TX 78701

EXAMINER	
MOSHER, MARY	

ART UNIT	PAPER NUMBER
1648	6

DATE MAILED: 10/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/880,609	Applicant(s) ZHANG ET AL.	
	Examiner Mary E. Mosher, Ph.D.	Art Unit 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *8/27/2001, 7/16/2003, 9/11/2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *30-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *30-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3, 6, 7* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

In this application, the handwritten list of file contents has an entry regarding "Pet. 1.53" filed 3/28/03, but there is no paper in the file with this date. Is there a paper missing, or is the entry in error?

Information Disclosure Statement

In the IDS filed 9/11/2003, reference C103 has not been considered, as a copy of this reference was not supplied.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 30-43 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 70-104 of copending Application No. 09/556,570 in view of March 5,552,309. Both these claims and the copending claims are drawn to purified recombinant adenovirus preparations. These claims differ from the copending claims in that they recite purity limitations and a total number of virus particles in the range of 5×10^{14} to 1×10^{18}, where the copending

claims recite only purity limitations. However, March teaches administering 10^{14} pfu of adenovirus to a host, see column 6 lines 50-52. Therefore a stock of adenovirus sufficient to administer to a handful of hosts is seen as obvious.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

Claims 30, 34, 35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 30 is indefinite because it depends from a cancelled claim. Claims 34-35 recite "a particle concentration" but do not recite any units. Are particles/ml intended?

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

In making prior art rejections, applicants are denied the benefit of prior applications 08/975,519 and 60/031,329, because these priority applications do not describe the claimed composition comprising between 5×10^{14} and 1×10^{18} viral particles. The disclosure in these parent documents includes the statement "The projected annual demand for a 300 clinic patient clinical trial could read approximately 6 $\times 10^{14}$ PFU." However, this statement does not reasonably convey the concept of one composition meeting or exceeding this annual demand, with the range limitations recited in the claims. Therefore, the effective date is seen as December 1, 1998, the filing date of 09/203,078.

Claims 30-40 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious Condon et al US 6,168,944. These claims are drawn to a "purified" composition comprising specified numbers of virus particles. The specification states on page 83: "The term "purified" as used herein, is

intended to refer to a composition, isolatable from other components, wherein the adenoviral particle is purified to any degree relative to its naturally-obtainable form. " Condon teaches production of recombinant adenovirus, and teaches "a total yield of viral particles of 1.4×10^{15} from each 160-L batch" and "about 3 to 4×10^{15} from each 160-L batch". See column 5, lines 30-48 and the Examples. Since even the total culture medium is purified relative to adenovirus as it is obtained in nature, the batch cultures of the Condon patent meet the claim limitations for the broadest claims. Furthermore, Condon concentrates 162 liters of culture lysate to 8-16 liters by ultrafiltration, thereby concentrating the virus at by least another log. Condon is silent upon the ratio of particles/pfu, and the amount of contaminating BSA in the final product. However, Condon does teach rapid removal of BSA at the first stage of harvest, see e.g. column 8, lines 1-15. Since Condon does not teach any harsh processing conditions, there is reason to believe the ratio of particles:PFU is similar to that found in a typical adenovirus culture lysate. Therefore, the product disclosed by Condon reasonably appears the same as, or similar to, the claimed product. Patent owner's burden under the circumstances presented herein was described in In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433-434 (CCPA 1977) as follows:

> Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. . . . Whether the rejection is based on `inherency' under 35 U.S.C. § 102, on `prima facie obviousness' under 35 U.S.C. § 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products [footnote omitted].

Claim 43 is rejected under 35 U.S.C. 103(a) as being unpatentable over Condon et al in view of Shabram et al WO 96/27677 (B2) or Hugyhe et al (C44). Condon teaches large-scale recombinant adenovirus preparations containing up to 4×10^{15} particles per batch. Condon differs from the claimed invention in that the virus preparations are not highly purified, and therefore unlikely to meet the claim limitation for eluting as essentially a single HPLC peak comprising 97-99% of the total area. Hugyhe teaches a chromatographic purification method for adenovirus that has a yield of 31%%. Purification of Condon's batch by the chromatography method of Hughye would result in a batch, meeting the recited purity requirement, with $>1 \times 10^{15}$ particles. Since both Condon and Hugyhe share the ultimate goal of producing recombinant virus suitable for gene therapy, it would have been obvious to combine the production method of Condon with the purification method of Hughye, with reasonable expectation of success. The invention as a whole is therefore prima facie obvious, absent unexpected results.

Claims 30, 31, 34, 36, 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hugyhe et al WO 96/27677 (B2) or Hugyhe et al (C44).. Hugyhe teaches highly purified recombinant adenoviruses, with a working example producing 7×10^{11} particles from 1.5 liters of media, and a particle/PFU ratio of 60-80. This differs from the claimed invention only in that the invention requires 1,000 to 10,000,000-fold more virus, in an unspecified volume. It would have been obvious to produce more virus, even more than a thousand-fold more virus, simply by growing larger batches and pooling the purified virus from multiple purification runs, with reasonable expectation of

success. One would have been motivated to pool the purified virus, to have a large and consistent stock for use in gene therapy protocols. Even if a brute-force approach would be expensive, it would still be obvious. Therefore, the invention as a whole is seen as prima facie obvious, absent unexpected results.

Claims 30-38, 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blanche et al WO98/00524 (B3). For convenience, reference is made to passages in the U.S. equivalent, 6,485,958 (A4). Blanche teaches highly purified recombinant adenoviruses, with working examples producing 1×10^{13} to 4×10^{14} particles, see columns 23-24, lines 17-56, and working examples with particle/PFU ratios of 20, see the table at columns 21-22. Again, this differs from the claimed invention only in that the invention requires a larger total amount of virus. It would have been obvious to produce more virus, simply by growing larger batches and/or pooling the purified virus from multiple purification runs, with reasonable expectation of success. One would have been motivated to pool the purified virus, to have a large and consistent stock for use in gene therapy protocols. Even if a brute-force approach would be expensive, it would still be obvious. Therefore, the invention as a whole is seen as prima facie obvious, absent unexpected results.

The following publication is cited as of interest: Phillips et al (C75) discusses an 8,000 liter batch mammalian cell culture, and mentions "the traditional technology involving the production of the appropriate viruses in large scale tissue cultures remains the most usual approach in vaccine manufacture."

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary E. Mosher, Ph.D. whose telephone number is 703-308-2926. The examiner can normally be reached on M-T and alternate F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Tuesday, September 30, 2003

MARY E. MOSHER
PRIMARY EXAMINER
GROUP 1800